

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Heinz-Josef LENZ et al.

Serial No.: 10/522,664

Group Art Unit: Not Yet Assigned

based on

Int'l Appl. No.: PCT/US2003/024065

Examiner: Not Yet Assigned

Int'l Filing Date: 31 July 2003

For: POLYMORPHISMS FOR  
PREDICTING DISEASE AND  
TREATMENT OUTCOME

## INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In accordance with 37 CFR §§ 1.97 and 198, the items identified in this Information Disclosure Statement (IDS) are being brought to the attention of the Office. The items are listed on the attached forms PTO/SB/08a and PTO/SB/08b. The Examiner is requested to make these documents of record.

The items identified in this IDS may or may not be "material" pursuant to 37 CFR § 1.56. The submission thereof by Applicants is not to be construed as an admission that any such patent, publication or other information referred to therein is material or considered to be material (37 CFR § 1.97(h)), or even qualifies as "prior art" under 35 USC § 102 with respect to this invention unless specifically designated by Applicants as such.

**1. Timing of the Information Disclosure Statement:**

☒ This IDS is believed to be timely in that it is being submitted under 37 CFR § 1.97(b), that is (1) with the new patent application submitted herein (37 CFR § 1.97(a)); or (2) within three months of the filing date of the application, which is not a continued prosecution application filed under § 1.53(d) or (3) within three months of entry of the national stage as set forth in 37 CFR § 1.491; or (4) before the mailing of a first Office action on the merits; or

(5) before the mailing of a first Office action after filing a request for continued examination under § 1.114. Thus, no fee is required.

- ☒ However, if the undersigned is in error in this regard, Applicant respectfully requests that the Office consider this IDS as filed under 37 CFR § 1.97(c), if applicable, and charge the fee due under 37 CFR § 1.17(p) to the deposit account referenced below.
- ☐ However, if the undersigned is in error in this regard, Applicant respectfully requests that the Office consider this IDS as filed under 37 CFR § 1.97(c), if applicable, and a statement under 37 CFR § 1.97(e) is included below, thus no fee is required.

☐ This IDS is being submitted under 37 CFR § 1.97(c), that is after mailing of a first Office Action on the merits, but before a Final Action under 37 CFR § 1.113 or a Notice of Allowance under 37 CFR § 1.311.

- ☐ The fee due under 37 CFR § 1.17(p) is submitted herewith.
- ☐ The fee due under 37 CFR § 1.17(p) is being concurrently submitted with the filing of an electronic IDS submission. Thus, no additional fee is required.
- ☐ A statement under 37 CFR § 1.97(e) is included below, thus no fee is required. In the event that this IDS is not received before a Final Action or a Notice of Allowance, then Applicant respectfully requests that the Office consider the filing of these papers to be submitted under 37 CFR § 1.97(d) and charge the fee due under 37 CFR § 1.17(p) to the deposit account below.

☐ This IDS is being submitted under 37 CFR § 1.97(d), that is after a Final Action under 37 CFR § 1.113 or a Notice of Allowance under 37 CFR § 1.311, but before payment of the issue fee. A statement under 37 CFR § 1.97(e) is included below. The fee due under 37 CFR § 1.17(p) is submitted herewith.

☐ This IDS is being submitted under 37 CFR § 1.97(i), that is after a Final Action under 37 CFR § 1.113 or a Notice of Allowance under 37 CFR § 1.311, but before payment of the issue fee.

**STATEMENT UNDER 37 CFR § 1.97(e):**

- ☐ No item contained in this IDS was cited in a communication from a foreign patent office in a counterpart foreign application more than three months prior to the filing of this IDS.
- ☐ No item contained in this IDS was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing this statement

after making reasonable inquiry, no item of information contained in this IDS was known to any individual designated in 37 CFR § 1.56(c) more than three months prior to the filing of this IDS.

## **2. Copies of the Cited Items:**

- ☒ Copies of all of the items listed on the attached forms PTO/SB/08a and PTO/SB/08b are enclosed.
- ☐ Copies of only the following items listed on the attached forms PTO/SB/08a (Item Nos. \*) and PTO/SB/08b (Item Nos. \*) are enclosed.
- ☐ Copies of the following items listed on the attached form PTO/SB/08a (Item Nos. \*) are not enclosed. See 37 CFR 1.98(a)(2)(i).
- ☐ Copies of the following documents listed in PTO/SB/08a (Item Nos. \*) and PTO/SB/08b (Item Nos. \*) are not supplied as they were previously cited by the Office or submitted in Information Disclosure Statements in related applications (Application No. \*, filed \*) and relied upon in this application for an earlier filing date under 35 USC § 120. See 37 CFR § 1.98(d). The Examiner is requested to make these documents of record.
- ☐ Copies of the following items listed on the attached forms PTO/SB/08a (Item Nos. \*) and PTO/SB/08b (Item Nos. \*) were cited in a foreign examination report in a related case. A copy of the search report and the cited references not already of record in this application are attached hereto.

## **3. Concise Explanation of Relevance:**

- ☒ A concise explanation of relevance of the items listed on forms PTO/SB/08a and PTO/SB/08b is not given.
- ☐ A concise explanation of relevance of [some of] the items listed on forms PTO/SB/08a and PTO/SB/08b is in the form of an English language copy of a Search Report from a foreign patent office, issued in a counterpart application, which refers to the relevant portions of the references (copy attached).

## **4. Related Applications:**

- ☐ Applicant(s) bring to the Office's attention the following related application(s): U.S. Patent Application No. \* filed \*, now U.S. Patent No. \*.

## 5. Conclusion:

Citation of the above documents shall not be construed as:


1. an admission that the documents are necessarily prior art with respect to the instant invention;
2. a representation that a search has been made, other than as described above; and
3. an admission that the information cited herein is, or is considered to be, material to patentability as defined in § 1.56(b).

It is respectfully requested that the Examiner indicate consideration of the cited references by returning a copy of the attached forms PTO/SB/08a and PTO/SB/08b with initials or other appropriate marks. In the unlikely event that the transmittal letter is separated from this document and the U.S. Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-2518** referencing 7000732001.

However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: August 3, 2005

By:   
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Substitute for form 1449A-PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

1

of

1

**Complete if Known**

Application Number

10/22,664

Int'l Filing Date

31 July 2003

First Named Inventor

Heinz-Josef LENZ

Art Unit

Not Yet Assigned

Examiner Name

Not Yet Assigned

Attorney Docket Number

US7000732001

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code <sup>2</sup> (if known)			
	1	US-5,705,336	01-06-98	Reed et al.	
	2	US-6,716,581 B2	04-06-04	Lenz et al.	
	3	US-2004/0067519 A1	04-08-04	Lenz et al.	
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**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> – Number <sup>4</sup> – Kind Code <sup>5</sup> (if known)				
	4	WO 01/36686 A2 & A3	05-25-01	University of Southern California		
	5	WO 01/75175 A2, R5 & A3	10-11-01	University of Southern California		
	6	WO 2004/011625 A2 & A3	02-05-04	University of Southern California		

Examiner's  
SignatureDate  
Considered

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

## Complete if Known

Substitute for form 1449B-PTO

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

1

of

3

Application Number

10/522,664

Int'l Filing Date

31 July 2003

First Named Inventor

Heinz-Josef LENZ

Art Unit

Not Yet Assigned

Examiner Name

Not Yet Assigned

Attorney Docket Number

US7000732001

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
	1	ABDEL-RAHMAN, S. et al. "Polymorphisms in DNA Repair Gene XRCC1 Increases the Risk of Colorectal Cancer in Egypt" <i>Proceedings of the American Association for Cancer Research</i> (March 2000) 41:595, No. 3791	
	2	BOARD, P.G. et al. "Isolation of a cDNA clone and localization of the human glutathione S-transferase 3 genes to chromosome bands 11q13 and 12q13-14" <i>Ann. Hum. Genet.</i> (1989) 53:205-213	
	3	CALDECOTT, K.W. et al. "XRCC1, A Central Regulator of Single Strand Break Repair and Base Excision Repair" <i>Proceedings of the American Association for Cancer Research</i> (March 2000) 41:891, No. 526	
	4	DUELL, E.J. et al. "Polymorphisms in the DNA repair genes XRCC1 and ERCC2 and biomarkers of DNA damage in human blood mononuclear cells" <i>Carcinogenesis</i> (May 2000) 21(5):965-971	
	5	DIVINE, K.K. et al. "The XRCC1 399 GLN Polymorphism: Potential Association with Lung Adenocarcinoma" <i>Proceedings of the American Association for Cancer Research</i> (March 2000) 41:591, No. 3762	
	6	EDLER, D. et al. "Thymidylate Synthase Expression: An Independent Prognostic Factor for Local Recurrence, Distant Metastasis, Disease-free and Overall Survival in Rectal Cancer" <i>Clinical Cancer Research</i> (April 2000) 6:1378-1384	
	7	HALPERN, J. "Maximally Selected Chi Square Statistics for Small Samples" <i>Biometrics</i> (December 1982) 38:1017-1023	
	8	HARRIES, L.W. et al. "Identification of genetic polymorphisms at the glutathione S-transferase Pi locus and association with susceptibility to bladder, testicular and prostate cancer" <i>Carcinogenesis</i> (1997) 18(4):641-644	
	9	HEIDELBERGER, C. et al. "Fluorinated Pyrimidines, A New Class of Tumour-Inhibitory Compounds" <i>Nature</i> (March 30, 1957) 179:663-666	
	10	HORIE, N. et al. "Functional Analysis and DNA Polymorphism of the Tandemly Repeated Sequences in the 5'-terminal Regulatory Region of the Human Gene for Thymidylate Synthase" <i>Cell Structure and Function</i> (1995) 20:191-197	
	11	HORIKOSHI, T. et al. "Quantitation of Thymidylate Synthase, Dihydrofolate Reductase, and DT-Diaphorase Gene Expression in Human Tumors Using the Polymerase Chain Reaction" <i>Cancer Res.</i> (Jan. 1, 1992) 52:108-116	

Examiner's  
SignatureDate  
Considered

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet **2** of **3****Complete if Known**

Application Number	10/522,664
Int'l Filing Date	31 July 2003
First Named Inventor	Heinz-Josef LENZ
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	US7000732001

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
	12	HOWIE, A.F. et al. "Glutathione S-transferase and glutathione peroxidase expression in normal and tumour human tissues" <i>Carcinogenesis</i> (1990) 11(3):451-458	
	13	HU, J.J. et al. "Genetic Polymorphism of DNA Repair in Human Prostate Cancer Risk" <i>Proceedings of the American Association for Cancer Research</i> (March 2000) 41:596, No. 3798	
	14	ISHIKAWA, Y. et al. "Dihydropyrimidine Dehydrogenase Activity and Messenger RNA Level May Be Related to the Antitumor Effect of 5-Fluorouracil on Human Tumor Xenografts in Nude Mice" <i>Clin. Cancer Res.</i> (April 1999) 5:883-889	
	15	LEICHMAN, C.G. et al. "Quantitation of Intratumoral Thymidylate Synthase Expression Predicts for Disseminated Colorectal Cancer Response and Resistance to Protracted-Infusion Fluorouracil and Weekly Leucovorin" <i>J. Clinical Oncology</i> (Oct. 1997) 15(10):3223-3229	
	16	MANNERVIK, B. "The Isoenzymes of Glutathione Transferase" <i>Adv. Enzymol.</i> (1985) 57:357-417	
	17	MILLER, R. and D. SIEGMUND "Maximally Selected Chi Square Statistics" <i>Biometrics</i> (Dec. 1982) 38:1011-1016	
	18	MOSCOW, J.A. et al. "Expression of Anionic Glutathione-S-transferase and P-Glycoprotein Genes in Human Tissues and Tumors" <i>Cancer Res.</i> (March 15, 1989) 49:1422-1428	
	19	NISHIMURA, T. et al. "Association between expression of glutathione-associated enzymes and response to platinum-based chemotherapy in head and neck cancer" <i>Chemico-Biological Interactions</i> (1998) 111-112:187-198	
	20	PETERS, W.H.M. et al. "Expression of Drug-Metabolizing Enzymes and P-170 Glycoprotein in Colorectal Carcinoma and Normal Mucosa" <i>Gastroenterology</i> (Aug. 1992) 103:448-455	
	21	SALONGA, D. et al. "Colorectal Tumors Responding to 5-Fluorouracil Have Low Gene Expression Levels of Dihydropyrimidine Dehydrogenase, Thymidylate Synthase, and Thymidine Phosphorylase" <i>Clin. Cancer Res.</i> (April 2000) 6:1322-1327	
	22	SINGH, S.V. et al. "Differential expression of glutathione S-transferase, glutathione peroxidase, and glutathione reductase in normal and malignant human breast tissues" <i>Cancer Letters</i> (1990) 51:43-48	
	23	STERN, M.C. et al. "DNA Repair Gene XRCC1 Polymorphisms, Smoking and Bladder Cancer Risk" <i>Proceedings of the American Association for Cancer Research</i> (March 2000) 41:592, No. 3771	
	24	SWEENEY, C. et al. "Association between Survival after Treatment for Breast Cancer and Glutathione S-Transferase P1 Ile <sup>105</sup> Val Polymorphism" <i>Cancer Res.</i> (Oct. 15, 2000) 60:5621-5624	

Examiner's  
SignatureDate  
Considered

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

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<p>Substitute for form 1449B-PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p><i>(use as many sheets as necessary)</i></p>				Complete if Known	
				Application Number	10/522,664
				Int'l Filing Date	31 July 2003
				First Named Inventor	Heinz-Josef LENZ
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
Sheet	3	of	3	Attorney Docket Number	US7000732001

[illegible]

Examiner's Signature		Date Considered	
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